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PRE-APPEAL BRIEF REQUEST FOR REVIEW		Docket Number (Optional) TNI 2-011	
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		First Named Inventor Jessie L.-S. Au	
		Art Unit 1614	Examiner James D. Anderson
<p>Applicant requests review of the final rejection in the above-identified application. No amendments are being filed with this request.</p> <p>This request is being filed with a notice of appeal.</p> <p>The review is requested for the reason(s) stated on the attached sheet(s). Note: No more than five (5) pages may be provided.</p>			
<p>I am the</p> <p><input type="checkbox"/> applicant/inventor.</p> <p><input type="checkbox"/> assignee of record of the entire interest. See 37 CFR 3.71. Statement under 37 CFR 3.73(b) is enclosed. (Form PTO/SB/98)</p> <p><input checked="" type="checkbox"/> attorney or agent of record. Registration number <u>13-4830</u></p> <p><input type="checkbox"/> attorney or agent acting under 37 CFR 1.34. Registration number if acting under 37 CFR 1.34 _____</p>		<p><u>/J.K. Mueller, Jr./</u> Signature Jerry K. Mueller, Jr. Typed or printed name 614-436-0600 Telephone number June 17, 2008 Date</p>	
<p>NOTE: Signatures of all the inventors or assignees of record of the entire interest or their representative(s) are required. Submit multiple forms if more than one signature is required, see below*.</p>			
<p><input type="checkbox"/> *Total of _____ forms are submitted.</p>			

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of : Jessie L.S.-Au, *et al.*
Serial No. : 10/807,620
Filed: : March 24, 2004
For: : METHODS AND COMPOSITIONS TO DETERMINE THE
CHEMOSENSITIZING DOSE OF SURAMIN USED IN
COMBINATION THERAPY
TC/AU : 1614
Examiner : James D. Anderson
Attorney Docket No. : TNI 2-011

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PRE-APPEAL BRIEF REQUEST FOR REVIEW

Sir:

DuPont discloses an anti-tumor composition composed of an anti-neoplastic agent and shark cartilage. One of the listed anti- neoplastic compositions is suramin. Not disclosed by DuPont is the fact that use of therapeutic (high) doses of suramin yield concentrations between about 300 to about 650 μM , which do not enhance the efficacy of chemotherapeutics and only enhanced the toxicity of chemotherapy. In fact, it was Applicants who showed that only low doses of suramin, which yield circulating concentrations of below about 200 μM (*e.g.*, between about 10 to about 50 μM plasma concentrations) when a chemotherapeutic agent (*e.g.*, paclitaxel) was present in the plasma at therapeutically significant levels, enhanced the efficacy of chemotherapy in tumor-bearing animals. Applicants' discovery is diametrically the opposite of the teachings of DuPont.

With respect to "print instructions", it is material error to ignore printed instructions in applying Section 103(a), even if the printed matter does not constitute patentable subject matter. *In re Gulack*, 217 USPQ 401 (Fed. Cir. 1983). More recently, the same Court stated that printed matter has patentable significance if there exists any new and unobvious functional relationship between the printed matter and the composition of the kit. *In re Ngai*, 35 USPQ2d 1384 (Fed. Cir. 2004). The MPEP expressly recognizes the vitality of the *Gulack* decision at MPEP § 2112.01 by stating, *inter alia*: "III. ... [T]he critical question is whether there exists any new and unobvious functional relationship between the printed matter and the substrate."

Applying that Court and MPEP sanctioned standard to the kit subject matter of claim 22, the printed instructions provide a new and unobvious functional relationship between suramin and the printed instructions. That is, the printed instructions inform the user that a patient must have a low dose of circulating suramin ($< 200 \mu\text{M}$) at which time a chemotherapeutic is administered to the patient for enhancement of the chemotherapeutic activity. Moreover, the printed instructions also provide an algorithm for the physician to use in determining the proper dose of suramin for each patient based on criteria not taught by DuPont or any other reference. Such criteria include the following elements from claim 22:

- (b1) determining the squared value of the body surface area (BSA) of said patient;
- (b2) determining the time elapsed, in days, since the initiation of the last suramin treatment; and
- (b3) calculating the dose of low dose suramin using a nomogram that shows the dose according to the parameters of squared value of body surface, and elapsed days since last suramin treatment.

All other claims include the limitations of claim 22. Claim 26 further discloses a particular cytotoxic agent. Claims 27 and 28 further disclose particular ranges of circulating suramin. A nomogram is recited in claim 30. Additional cytotoxic agents are disclosed in claim 31. Claim 32 further discloses a time period over which the suramin is administered to the patient. Claim 33 also discloses a time period over which particular amounts of suramin are administered to the patient. Finally, claim 34 further discloses another treatment regimen.

None of these functional relationships between suramin and the printed instructions are disclosed in the art.

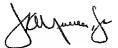
In support of this position a declaration dated March 6, 2008 of Dr. Au, a co-inventor of the subject matter disclosed in the above-identified application, was submitted. Dr. Au elegantly relates the research that led to the subject being claimed. In particular, Dr. Au supports each every point argued above. Indeed, there is the requisite functional relationship between suramin and the printed instructions. Moreover, in Dr. Au's expert opinion, the functional relationship is non-obvious.

The printed instructions, then, satisfy the *Gulack* test as approved of in the MPEP and should not have been ignored by the Examiner. It is noted finally that even Ngai's ultimately issued patent contained a "kit" claim.

Conclusion

Applicants respectfully request that the final rejection of the Examiner be reversed and that the claims be allowed and this application passed to issue.

Respectfully submitted,



Date: 17 June 2008

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